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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,164	11/26/2003	Stephan R. Targan	066783-0142	8299

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Cathryn Campbell
McDERMOTT, WILL & EMERY
Suite 700
4370 La Jolla Village Drive
San Diego, CA 92122

EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,164	TARGAN ET AL.	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,26 and 29-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,26 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/03/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 25-26 and 29-31 are pending.

2. Applicant's election of Group I, claims 25-26 and 29 and newly added claims 30-31, without traverse, in the reply filed on 10/24/2006 is acknowledged.

3. Claims 1-24 and 27-28 are cancelled.

4. Claims 25-26 and 29-31 are currently under consideration as they read on a method of determining a risk of having or developing a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery in a subject having Crohn's disease, comprising determining the presence or absence of three markers in the subject, said three markers being IgA anti-I2 antibodies, anti-Saccharomyces cerevisiae antibodies (ASCA), and IgA anti-OmpC antibodies.

5. Applicant's IDS filed on 11/03/2004 is acknowledged.

Claim Rejections - 35 USC § 101

6. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

7. Claims 25-26 and 29 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-24 of copending Application No. 10/413,501. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The scope of the claimed subject matter is identical.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 25-26 and 29-31 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: obtaining a sample comprising the IgA anti-I2, ASCA and anti-OmpC antibodies from the subject. There is no description in the specification for in vivo assays to detect circulating antibodies. As such, in vitro assays require isolating a sample with the analyte to be detected.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 25-26 and 29-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant is not enabled for: A method of determining a risk of having or developing a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery in a subject having Crohn's disease, comprising determining the **presence or absence** of three markers in the

subject, said three markers being IgA anti-I2 antibodies, anti-Saccharomyces cerevisiae antibodies (ASCA), and IgA anti-OmpC antibodies.

Vasiliauskas et al (Reference 30, IDS filed on 11/03/2004), a reference with a common inventor with the instant application, states on pages 490-492, there is a great variation in levels of marker antibody expression among Crohn's disease patients and the presence and levels of specific marker antibody could reflect distinct immunological reactivity leading to differences in clinical expression among Crohn's disease patients. On page 492, the reference teaches that "not only the type, but the magnitude of the immune marker expression (as measured by level of host marker antibody production) may reflect divergent immune responses that manifest as specific disease behaviors (phenotypes) in these subsets of CD patients." In fact, the reference results showed that only 'Higher levels of ASCA were associated with fibrostenosing disease, internal penetrating disease and less often UC-like features (table 3) " (first full paragraph on page 492). The results of the study showed "the significance of taking into account the magnitude of the host immune response-that is, higher levels of ASCA and pANCA expression to identify CD subgroups that are immunologically and clinically homogeneous." (conclusion, page 494). The Landers et al. reference (Reference 17, IDS filed on 11/03/2004) also shows support for determining the magnitude as well as the presence of individual seroactivity to relate to disease behavior in CD patients (page 695, second paragraph of the discussion). Therefore, the specification's disclosure is not enabling for a method of determining a risk of having or developing a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating disease

or the need for small bowel surgery based only upon presence or absence of the markers, as evidenced by the prior art which states that the magnitude or level of the antibody marker is important for disease subtype classification.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method of determining a risk of having or developing a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery in a subject having Crohn's disease, comprising determining the **presence or absence** of three markers in the subject, said three markers being IgA anti-I2 antibodies, anti-Saccharomyces cerevisiae antibodies (ASCA), and IgA anti-OmpC antibodies. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 25-26 and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Targan et al. (PTO-892, Reference U) in view of Vasiliauskas et al. (Reference 30, IDS filed on 11/03/2004) and Landers et al. (Reference 17, IDS filed on 11/03/2004).

Targan et al., teaches detecting the presence of anti-I2, ASCA and anti-OmpC IgA molecules in a clinical subtype (antibiotic reactive) of Crohn's patients by ELISA. The study of a cohort of patients with ilieal or illeal with right sided colonic Crohn's disease showed that patient serum antibody reactivity clustered into one of four groups with antibiotic-induced remission percentages correlating with the presence or absence of the markers.

The claimed invention differs from the prior art by the recitation of a step of determining the magnitude of three markers in the subject further comprises a step of performing quartile analysis of the magnitude of each marker; and wherein quartile analysis further comprises assigning scores based on the quartile into which a marker falls and then adding the scores to obtain a quartile sum score whereby a higher quartile sum score indicates a greater risk of having or developing said clinical subtype

characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery.

Vasiliauskas et al. teaches detecting ASCA and ANCA antibodies as a tool to stratify Crohn's disease into immunologically homogenous subgroups with distinct clinical characteristics including fibrostenosis, internal perforating disease and the need for small bowel surgery and that Crohn's diease behaviour patterns are not mutually exclusive. ('Assessment of clinical characteristics' section pages 488-489). Statistical analysis was performed. The antibody levels were normalized and compared. Marker levels predicted Crohn's disease clinical characteristics (abstract, page 493, first paragraph of discussion and throughout results).

Landers et al. teaches detecting OpmC, ASCA and anti-I2 antibodies to determine a clinical subtype (loss of tolerance to microbial antigens). The markers were measured and quartile analysis was performed to determine the relationship between the marker antibodies in the Crohn's disease cohort (Figure 2). A number was assigned to each quartile and the sum of the quartiles was correlated to reactivity (paragraph spanning pages 693-694).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the quartile analysis of Crohn's disease markers method with determining the quartile sum score of Landers et al. to the method of determining

the correlation of Crohn's disease markers to clinical outcomes of Targan et al. and Vasiliauskas et al. to obtain the claimed claimed invention. .

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because "stratification based on CD behavior has been widely studied and reported" (page 494, 1st full paragraph) and "using selective expression of markers was demonstrated as a complementary approach for indentification of immunologically and clinically homogeneous subgroups" (p. 493, 1st paragraph of the discussion) as taught by Vasiliauskas et al. The statistical techniques of Landers et al. including quartile analysis with quartile sum scores simply demonstrated a useful method known in the art to analyze the antibody marker magnitude and prevalence data. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 17, 2007

Nora M. Rooney, M.S., J.D.

Patent Examiner

Technology Center 1600

MICHAIL BELYAVSKYI, PH.D.
PATENT EXAMINER

1/19/07